Atty. Dkt. No. 076333-0323

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant:	William E. KLUNK et al.
Title:	***BENZOTHIAZOLE DERIVATIVE COMPOUNDS, COMPOSITIONS AND USES***
Appl. No.:	10/645,847
Filing Date:	8/22/2003
Examiner:	Dameron Levest Jones
Art Unit:	1618
Confirmation Number:	8143

BRIEF ON APPEAL

Mail Stop Appeal Brief - Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Under the provisions of 37 C.F.R. § 41.37, Appellants file this Appeal Brief with a credit card payment form in the amount of $510, covering fee mandated by 37 C.F.R. 41.20(b)(2). If this fee is deemed to be insufficient, authorization is hereby given to charge any deficiency (or credit any balance) to the undersigned deposit account 19-0741.

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I. REAL PARTY IN INTEREST

The real party in interest is the UNIVERSITY OF PITTSBURGH, which acquired rights to the present application through an assignment recorded on October 26, 2005, at reel/frame No. 017139/0729.

II. RELATED APPEALS AND INTERFERENCES

There are no appeals or interferences related to the present application.

III. STATUS OF CLAIMS

Pending claims: 1-27.

Rejected claims: 1.

Objected to claims: 2-27.

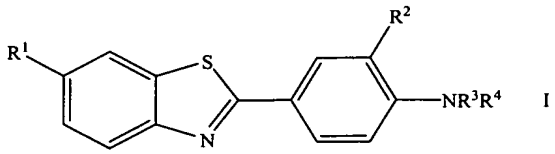
Appealed claims: 1.

IV. STATUS OF AMENDMENTS

Appellants last amended the claims in their response filed on April 21, 2008. According to the Advisory Action mailed on May 6, 2008, the claim amendments were entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Appealed claim 1 is directed to a compound that conforms to formula I:



I

or to a pharmaceutically acceptable salt, hydrate, solvate or prodrug of the compound.[1] Substituent R^1 is hydrogen, -OH, $-NO_2$, -CN, -COOR, $-OCH_2OR$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy or halo, where R is C_1-C_6 alkyl.[2] Substituent R^2 is a non-radioactive halo or a radioactive halo.[3] Substituent R^3 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl.[4]

Substituent R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl. In R^4, the alkyl, alkenyl or alkynyl comprises a radioactive carbon or is substituted with a radioactive halo when R^2 is a non-radioactive halo.[5]

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[1] *See* specification at page 5, lines 15-18.

[2] *Id.* at page 5, lines 19-20.

[3] *Id.* at page 5, line 23.

[4] *Id.* at page 6, line 1.

[5] *Id.* at page 6, lines 2-4.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The only appealed ground for rejection is the allegation that claim 1 is unpatentable, under the doctrine of obviousness-type double patenting, over claim 4 of co-owned U.S. Patent No. 7,270,800.

VII. ARGUMENT

The Board should reverse the PTO's rejection because the issuance of claim 1 would not manifest an improper time-wise extension of U.S. Patent No. 7,279,800 ("the '800 patent"), that is, because the claimed compounds are not obvious variants of cited claim 4. Well-settled law states that

> [a] nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s).[6]

Where, as here, the application at issue is the later filed application, only a one-way determination of obviousness is needed in resolving the issue of double patenting, *i.e.*, whether the invention defined in a claim in the application would have been anticipated by, or an obvious variation of, the invention defined in a claim in the patent.[7] Further, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. § 103 obviousness determination.[8] Hence, the PTO must engage in the factual inquiries set forth in *Graham v. John Deere.*[9]

In the context of claims drawn to chemical compounds, the PTO's reviewing court stated that

> [a] known compound may suggest its homolog, analog, or isomer because such compounds "often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." We clarified, however, that in order to find a prima facie case of unpatentability in such instances, a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required.[10]

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[6] *See, e.g., In re Kaplan,* 789 F.2d 1574, 229 U.S.P.Q. 678 (Fed. Cir. 1986); *In re Berg,* 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman,* 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir., 1993); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). *See also* MPEP § 804(II)(B)(1) (Rev. 5, Aug. 2006).

[7] *See In re Berg, supra.*

[8] *In re Braat,* 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir., 1991); *In re Longi, supra.*

[9] *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). *See* Applicants' Response filed on December 18, 2007 at page 8.

[10] *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356, 83 U.S.P.Q.2d 1169, 1174 (Fed. Cir. 2007) (internal citations omitted; citing *In re Deuel,* 51 F.3d 1552, 1558 (Fed.Cir.1995)).

"Thus in cases involving new chemical compounds, *it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.*" [11]

A. Structural Requirements in Claim 4 of the '800 Patent Teach Away from the Species of Rejected Claim 1

Claim 4 of the '800 patent is directed to a method of synthesizing certain benzothiazole compounds designated as Nos. 1-34, 36, and 38-45, wherein at least one of the atoms in each of the compounds is replaced by a halogen isotope, specifically ^{131}I, ^{125}I, ^{123}I, ^{76}Br, ^{18}F, or ^{19}F. The cited claim does not specify, however, at what position(s) on the recited benzothiazole compounds the replacement must occur, nor does the claim, by itself, suggest any such positions. Thus, the choices of (1) a specific halogen isotope and (2) the position on a benzothiazole where that isotope is to reside give rise to myriad possible combinations of (1) and (2). With this factual background, the PTO settled upon the unguided selection of just that one possible combination from cited claim 4 in which a "radiohalogen may be present at position R2 as in the instant invention."[12]

The PTO's analysis fails to account for a much larger group of compounds that fall *outside the scope of rejected claim 1* by virtue of radiohalogen substitution occurring at positions other than present R^2.[13] In other words, the method of cited claim 4 results in many more compounds falling outside rather than within the scope of rejected claim 1.

To illustrate, the PTO drew particular attention to compound 2, *inter alia*, in cited claim 4 that bears a 2-iodo substituent, which substituent corresponds to R^2 in rejected claim 1.[14] Yet, cited compound 2 features at least nine (9) positions including R^2 where an existing atom can be replaced by one of the halogen isotopes recited by claim 4 of the '800 patent. Based upon these mere possibilities, claim 4 no more hints at substitution at the 2-position (R^2 in rejected claim 1) than any other position, the presence of halogens at the 2-position in some compounds notwithstanding.[15]

The balancing of possibilities in cited claim 4 – radiohalogen at R^2 *versus* radiohalogen elsewhere – are tipped heavily in favor of the latter by dint of numerical superiority. Such imbalance

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[11] *Id.* (emphasis added).

[12] Final Office Action mailed October 18, 2007 at page 2.

[13] *See* Applicants' Response filed on December 18, 2007 at page 8.

[14] *See* Final Office Action mailed October 18, 2007 at page 2.

[15] *See* Applicants' Response filed on April 21, 2008 at page 8.

is tantamount to claim 4 teaching away from the claimed invention.[16] Viewed in this light, present claim 1 is not obvious over cited claim 4.

B. The PTO Impermissibly Relied Upon Hindsight Knowledge of Rejected Claim 1 in Concluding that Substituent R^2 Being a Radiohalogen is an Obvious Variant

Apparently responsive to Appellants' objection to the foregoing factual errors above running throughout the PTO's analysis, the PTO propounded a novel legal theory of obviousness that must fail for its ultimate reliance upon hindsight knowledge of Appellants' invention. In the PTO's own words:

> [T]he skilled artisan would recognize that if *the instant invention discloses a radiohalogen at position R2* and the patented invention disclose [*sic*] that the atoms of the Compounds [*sic*] are replaced with a radiohalogen and some of the Compounds [*sic*] are *ones which have a halogen at the same position as R2 (instant invention)*, then the Patent and Trademark Office did not seize upon the mere possibility that a radiohalogen could reside on the position corresponding to R2 in the present invention.[17]

In the quote above, the italicized passages lay bare the PTO's legal error: the Office would imbue the skilled artisan with knowledge of Appellants' claim 1. Specifically, "[b]y this flawed approach, the PTO would have the artisan refine a selection of radiohalogens and substitution patterns in cited claim 4, such selection being unprincipled but for the specific requirements of present formula I, *i.e.*, R^2 must be [a] non-radioactive or radioactive halo substituent."[18] Stripped of this impermissible hindsight knowledge, the PTO's obviousness analysis reduces inevitably to the "mere possibility" the PTO seeks in vain to avoid.

Under the correct rule of law, by contrast, the PTO must articulate "a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention'."[19] The PTO's "mere possibility" is antithetical to the requisite "showing" that would, but ultimately cannot, establish how claim 4 of the '800 patent would suggest the "specific modifications" to the recited benzothiazoles so as to result in the presently claimed benzothiazoles bearing radiohalogens at R^2.

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[16] *See* Applicants' Response filed on December 18, 2007 at page 9

[17] Advisory Action mailed on January 14, 2008 at page 2 (emphasis added).

[18] Applicants' Response filed on April 21, 2008 at page 7.

modifications" to the recited benzothiazoles so as to result in the presently claimed benzothiazoles bearing radiohalogens at R^2.

The PTO recognized in this context that some compounds in cited claim 4 bear non-radiohalogens corresponding to present R2, and the PTO therefore advanced the proposition that replacing "the non-labeled halogen . . . with a radiolabeled halogen . . . is an obvious variant of the patented invention."[20] What is precisely missing is, again, an articulation of why the replacement is obvious. It is not enough under the principles above to simply state that Appellants' invention is an obvious extrapolation of the '800 patent.

For instance, the PTO's analysis fails to specify why the skilled artisan would first select a benzothiazole in claim 4 of the '800 patent bearing a non-radioactive halogen substituent at the 2-position, corresponding to present R^2. As far as Appellants are aware, there is no rule of patent law holding that atom isotopes are *prima facie* obvious variants of each other. Thus, to further illustrate, no chemical or legal principle would manifest a preference for a compound in cited claim 4 bearing F at the 2-position any more than a compound bearing H at the position.

* * *

For the reasons above, claim 1 is not obvious over claim 4 of the '800 patent, and so patenting the former would not result in an impermissible time-wise extension of the latter. Accordingly, Appellants respectfully request the Board to reverse the PTO's ground for rejection.

Respectfully submitted,

Date June 19, 2008 By Steven M. Reid

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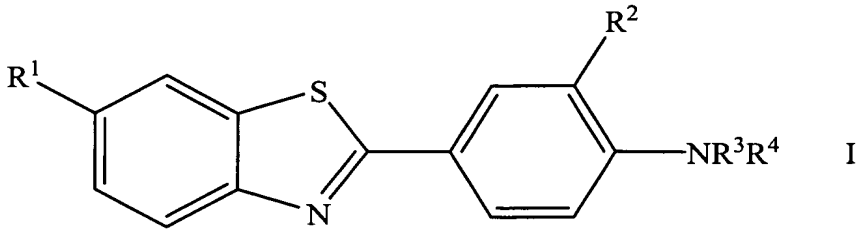
Attorney for Applicant
Registration No. 54,393

[20] Advisory Action mailed on January 14, 2008 at page 2.

VIII. CLAIMS APPENDIX

1. (Previously presented) A compound of formula I



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or a pharmaceutically acceptable salt, hydrate, solvate or prodrug of the compound, wherein:

R^1 is hydrogen, -OH, $-NO_2$, -CN, -COOR, $-OCH_2OR$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy or halo;

R is C_1-C_6 alkyl;

R^2 is a non-radioactive halo or a radioactive halo;

R^3 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl; and

R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl, wherein the alkyl, alkenyl or alkynyl comprises a radioactive carbon or is substituted with a radioactive halo when R^2 is a non-radioactive halo.

IX. EVIDENCE APPENDIX

1. Declaration pursuant to 37 C.F.R. § 1.132 filed and entered into the record on May 18, 2006.

2. Declaration pursuant to 37 C.F.R. § 1.132 filed and entered into the record on April 9, 2007.

X. RELATED PROCEEDINGS APPENDIX

None.

Atty. Dkt. No. 076333-0323

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: William E. KLUNK, Chester A. MATHIS, *et al.*

Title: ***BENZOTHIAZOLE DERIVATIVE COMPOUNDS, COMPOSITIONS AND USES***

Appl. No.: 10/645,847

Filing Date: 8/22/2003

Examiner: Dameron Levest Jones

Art Unit: 1618

DECLARATION UNDER 37 C.F.R. 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, William E. Klunk, and I, Chester A. Mathis, being duly warned, hereby declare that:

1. We are co-inventors of the invention disclosed and claimed in the captioned application.

2. The subject matter disclosed and claimed in the captioned application was invented by ourselves and Yanming Wang (who is no longer employed by the University of Pittsburgh).

3. We are co-authors of an academic publication by Mathis *et al.*, 46 *J. Med. Chem.* (2003) 2740-54 ("the Mathis publication"), which, we understand, the examiner of the captioned application has cited in an Office Action mailed January 26, 2006.

4. We also understand that the Mathis publication forms the basis of the examiner's rejecting claims 1-3 and 14 of the captioned application.

5. The co-authors of the Mathis publication who are other than the present inventors, namely, Daniel P. Holt, Guo-Feng Huang, and Manik L. Debnath, did not make contributions to subject matter claimed in the captioned application. Co-authors Holt, Huang, and Debnath

were assistants who carried out experiments under our direction in our capacity as the research principals for the publication.

6. Co-authorship was appropriate academic recognition of the contributions of Holt, Huang, and Debnath to the research reported in the Mathis publication. Nevertheless, the disclosures of the Mathis publication that, we understand, the examiner has invoked in rejecting the aforementioned claims, particularly in relation to "compound 19" of the Mathis publication, represent the work of the co-inventors alone.

7. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the captioned application or any patent resulting from that application.

5-2-06
Date

William E. Klunk

5-2-06
Date

Chester A. Mathis

Atty. Dkt. No. 076333-0323

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P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, William E. Klunk, and I, Chester A. Mathis, being duly warned, hereby declare that:

1. We are co-inventors of the invention disclosed and claimed in the captioned application.

2. The subject matter disclosed and claimed in the captioned application was invented by Chester A. Mathis, Yanming Wang, and myself.

3. We are co-authors of an academic publication by Wang *et al.*, 46 *J. Molecular Neuroscience* (2002) 11-16 ("the Wang publication"), which, we understand, the examiner of the captioned application has cited in an Office Action mailed January 17, 2007.

4. We also understand that the Wang publication forms the basis of the examiner's rejecting claims 1, 4, 8, 9, and 14 of the captioned application.

5. The co-authors of the Wang publication who are other than the present inventors, namely, Daniel P. Holt, Guo-Feng Huang, and Manik L. Debnath, did not make contributions to subject matter claimed in the captioned application. Co-authors Holt, Huang, and Debnath

were assistants who carried out experiments under our direction in our capacity as the research principals for the publication.

6. Co-authorship was appropriate academic recognition of the contributions of Holt, Huang, and Debnath to the research reported in the Wang publication. Nevertheless, the disclosures of the Wang publication that, we understand, the examiner has invoked in rejecting the aforementioned claims, particularly in relation to "compound 6" of the Wang publication, represent the work of the co-inventors alone.

7. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the captioned application or any patent resulting from that application.

April 3, 2007
Date

William E. Klunk

4/3/07
Date

Chester A. Mathis